

Substitute for form 1449B-PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 1 of 15

**Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 <del>1015</del> / 6 23
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
me	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
	3	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14:59-73	
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	6	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous p110 <sup>RB</sup> , the retinoblastoma tumor suppressor protein" <i>Oncogene</i> (1995) 10:697-704	
	7	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> (1988) 29(23):2855-2858	
	8	ASAKURA and ROBINS "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" <i>J. Org. Chem.</i> (1990) 55:4928-4933	
	9	ARISI et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" <i>Antivir. Res.</i> (1983) 3:161-174	
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	12	BALZARINI et al. "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" <i>Meth. Find. Exp. Clin. Pharmacol.</i> (1985) 7(1):19-28	
me	13	BALZARINI et al. "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (E)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" <i>Mol. Pharmacol.</i> (1987) 32:410-416	

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Signature

L. E. Crane

Date  
Considered

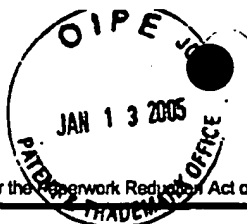
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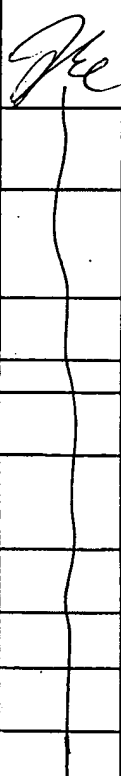
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First Named Inventor	H. Michael SHEPARD
Art Unit	1623 <del>1615</del> 1623
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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	14	BALZARINI et al. "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine , 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antihertepic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> (1993) 268(9):6332-6337	
	15	BALZARINI et al. "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" <i>Biochem. Biophy. Res. Co.</i> (1996) 225:363-369	
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	17	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42(4):457-464	
	18	BANERJEE et al. "Role of E2F-1 in chemosensitivity" <i>Cancer Res.</i> (Oct. 1, 1998) 58:4292-4296	
	19	BARBATO, et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4,3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1991) 10(4):853-866	
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	23	BARR et al. "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochemistry</i> (1983) 22:1696-1703	
	24	BARRETT "Trapping of the C5 methylene intermediate in thymidylate synthase" <i>J. Am. Chem. Soc.</i> (1998) 120:449-450	
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SignatureL. E. Crane Date  
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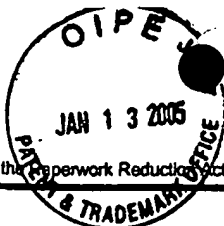
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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 15

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First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

### NON PATENT LITERATURE DOCUMENTS

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Me	26	BERGSTROM et al. "C-5-substituted pyrimidine nucleosides. 3. Reaction of allylic chlorides, alcohols, and acetates with pyrimidine nucleoside derived organopalladium intermediates" <i>J. Org. Chem.</i> (1981) 46(7):1432-1441	
Me	27	BERGSTROM et al. "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine and related analogues: Potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine against herpes simplex virus type 1" <i>J. Med. Chem.</i> (1984) 27:279-284	
Me	28	BERKOW et al. (eds); <i>The Merck Manual of Diagnosis and Therapy</i> , 16th Edition, Merck & Co., Rahway, NJ, (May 1992) only page 1278 supplied	
Me	29	BERTINO et al. "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> (1996) 14:5-9	
Me	30	BIGGE et al. "Palladium-catalyzed coupling reactions of uracil nucleosides and nucleotides" <i>J. Amer. Chem. Soc.</i> (Mar. 12, 1980) 102(6):2033-2038	
Me	31	BLACKLEDGE "New developments in cancer treatment with the novel thymidylate synthase inhibitor raltitrexed ('Tomudex')" <i>British J. Cancer</i> (1998) 77(Supp 2):29-37	
Me	32	BOSSLET et al. "A novel one-step tumor-selective prodrug activation system" <i>Tumor Targeting</i> (1995) 1:45-50	
Me	33	BOSSLET et al. "Elucidation of the mechanism enabling tumor selective prodrug monotherapy" <i>Cancer Res.</i> (Mar 15, 1998) 58:1195-1201	
Me	34	BRISON "Gene amplification and tumor progression" <i>Biochim. Biophys. Acta</i> (1993) 1155:25-41	
Me	35	CARL et al. "Protease-activated 'prodrugs' for cancer chemotherapy" <i>PNAS USA</i> (April 1980) 77(4):2224-2228	
Me	36	CARRERAS and SANTI "The catalytic mechanism and structure of thymidylate synthase" <i>Annu. Rev. Biochem.</i> (1995) 64:721-762	
Me	37	CARTER et al. "Humanization of an anti-p185 <sup>HER2</sup> antibody for human cancer therapy" <i>PNAS USA</i> (May 1992) 89:4285-4289	
Me	38	CAVA and LEVINSON "Thionation reactions of Lawesson's reagents" <i>Tetrahedron</i> (1985) 41(22):5061-5087	
Me	39	CHAKRAVARTY et al. "Plasmin-activated prodrugs for cancer chemotherapy. 2. Synthesis and biological activity of peptidyl derivatives of doxorubicin" <i>J. Med. Chem.</i> (1983) 26(5):638-644	
Me	40	CHAUDHURI and KOOL "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> (1995) 117:10434-10442	

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Signature

L. E. Crane

Date  
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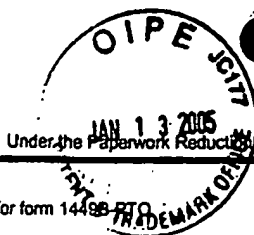
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		Filing Date	November 28, 2002		
		First Named Inventor	H. Michael SHEPARD		
		Art Unit	1623 ---1615---		
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JEC	41	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56:1331-1340	
	42	CHO and JOHNSON "(E)-5-(3-oxopropen-1-yl)-2'-deoxyuridine and (E)-5-(3-oxopropen-1-yl)-2',3'-dideoxyuridine; New antiviral agents: Synthesis and biological activity" <i>Tetrahedron Lett.</i> (1994) 35(8):1149-1152	
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JEC	53	DALE et al. "The synthesis and enzymatic polymerization of nucleotides containing mercury: Potential tools for nucleic acid sequencing and structural analysis" <i>PNAS USA</i> (August 1973) 70(8):2238-2242	
	54	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> " <i>J. Biol. Chem.</i> (1989) 264(16):9145-9148	
JEC	55	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> . (Additions and corrections)" <i>J. Biol. Chem.</i> (Dec. 2, 1994) 269(48):30740	

Examiner's Signature	L. E. Crane	Date Considered	09/21/2005
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<i>See</i>	56	DeCLERCQ et al. "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <i>J. Med. Chem.</i> (1983) 26:661-666	
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	58	DIRVIN et al. "The role of human glutathione S-transferase isoenzymes in the formation of glutathione conjugates of the alkylating cytostatic drug thiotepa" <i>Cancer Res.</i> (April 15, 1995) 55:1701-1706	
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<i>See</i>	63	EISENBRAND et al. "An approach towards more selective anticancer agents" <i>J. Synthetic Organic Chem.</i> (1996) 10:1246-1258	
**	64	EVARD et al. "An <i>in vitro</i> nucleoside analog screening method for cancer gene therapy" <i>Cell Biol. Toxicol.</i> (1996) 12:345-350	
<i>See</i>	65	EVARD et al. "An <i>in vitro</i> nucleoside analog screening method for cancer gene therapy" <i>Chem. Abstracts</i> (1996) 126:Abstract No. 26514	
	66	FARQUHAR et al. "Synthesis and antitumor evaluation of bis[(pivaloyloxy)methyl] 2'-deoxy-5-fluorouridine 5'-monophosphate (FdUMP): A strategy to introduce nucleotides into cells" <i>J. Med. Chem.</i> (1994) 37:3902-3909	
	67	FARQUHAR et al. "5'-[4-pivaloyloxy]-1,3,2-dioxaphosphorinan-2-yl]-2'-deoxy-5-fluorouridine: A membrane-permeating prodrug of 5-fluoro-2'-deoxyuridylic acid (FdUMP)" <i>J. Med. Chem.</i> (1995) 38:488-495	
	68	FARRUGIA et al. "Single agent infusional 5-fluorouracil is not effective second-line therapy after raltitrexed (Tomudex®) in advanced colorectal cancer" <i>Eur. J. Cancer</i> (1998) 34(7):987-991	
	69	FELIP et al. "Overexpression of c-erbB-2 in epithelial ovarian cancer" <i>Cancer</i> (Apr. 15, 1995) 75(8):2147-2152	
<i>See</i>	70	FINCH "Radiation Injury" In: <i>Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) 2204-2208	

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L. E. Crane

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Sheet 6 of 15

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623---=1615----
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
JEC	71	FINER-MOORE et al. "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> (1993) 232:1101-1116	
	72	FINER-MOORE et al. "Crystal structure of thymidylate synthase from T4 phage: Component of a deoxynucleoside triphosphate-synthesizing complex" <i>Biochemistry</i> (1994) 33:15459-15468	
XX	73	<del>FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>J. Invest. Dermatol.</i> (May 1990) 94(5):657-661</del>	
JEC	74	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>Chem Abstracts</i> (1990) 113:Abstract No. 254	
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	76	FRIES et al. "Synthesis and biological evaluation of 5-fluoro-2'-deoxyuridine phosphoramidate analogs" <i>J. Med. Chem.</i> (1995) 38(14):2672-2680	
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L. E. Crane

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<i>See</i>	87	HANDFIELD and LEVESQUE "Strategies for isolation of in vitro expressed genes from bacteria" <i>FEMS Microbiol. Revs.</i> (1999) 23:69-91	
**	88	HAKIMELAHJI et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
<i>See</i>	89	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235:448-455	
	90	HARRIS et al. "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Cancer Gene Ther.</i> (1996) 3(2):121-130	
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	92	HEIDELBERGER et al. "Fluorinated pyrimidines and their nucleosides" <i>Adv. Enzymol. Related Areas Mol. Biol.</i> (1983) 54:57-119	
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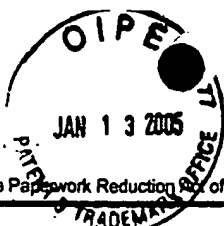
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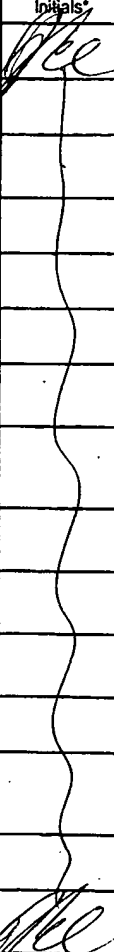
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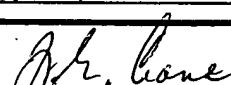
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	100	HU et al. "Determination of absorption characteristics of AG337, a novel thymidylate synthase inhibitor, using a perfused rat intestinal model" <i>J. Pharmaceutical Sciences</i> (July 1998) <b>87(7):886-890</b>	
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E. Crane 

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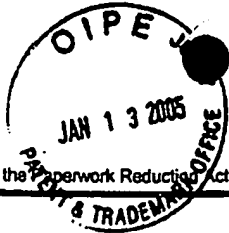
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First Named Inventor

H. Michael SHEPARD

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JPC	115	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40(5):359-363	
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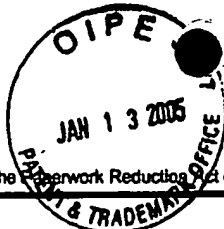
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10/048,033 - PTO-1449 #3

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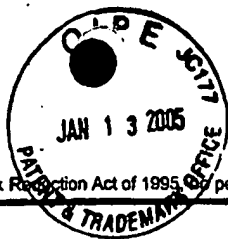
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Substitute for form 1449B-PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/048,033
		Filing Date	November 28, 2002
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1623 <del>==1615==</del>
		Examiner Name	Not Yet Assigned
Sheet 11 of 15	Attorney Docket Number	NB 2006.01	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T <sup>2</sup>
<i>[Signature]</i>	146	MONTFORT and WEICHSEL "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> (1997) 76(1-3):29-43	
<i>[Signature]</i>	147	MONTGOMERY et al., "Phosphonate analogue of 2'-deoxy-5-fluorouridylic acid" <i>J. Med. Chem.</i> (1979) 22(1):109-111	
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<i>[Signature]</i>	149	MORRISON & BOYD (eds) <i>Organic Chemistry</i> , Allyn & Bacon, Inc., Boston, MA, (1973) only pages 1170-1180 supplied	
<i>[Signature]</i>	150	MURAKAMI and SEKIYA "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> (1998) 400(1-2):421-437	
<i>[Signature]</i>	151	NAESENS et al. "Anti-HIV activity and metabolism of phosphoramidate derivatives of D4T-MP with Variations in the amino acid moiety" Poster Session 1, <u>The Tenth International Conference on Antiviral Research</u> , Hotel Nikko, Atlanta, GA April 6-11, 1997; published in <i>Antivir. Research</i> (April 1997) 34(2):A54 (Abstract 40)	
<i>[Signature]</i>	152	NAKANO et al., "Critical role of phenylalanine 34 of human dihydrofolate reductase in substrate and inhibitor binding and in catalysis" <i>Biochemistry</i> (1994) 33:9945-9952	
<i>[Signature]</i>	153	NICHOL and HAKALA "Comparative growth-inhibitory activity of homofolic acid against cell lines sensitive and resistant to amethopterin" <i>Biochem. Pharmacol.</i> (Oct. 1966) 15(10):1621-1623	
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<i>[Signature]</i>	159	PERRY et al. "Plastic adaptation toward mutations in proteins: Structural comparison of thymidylate synthases" <i>Proteins</i> (1990) 8:315-333	
<i>[Signature]</i>	160	PESTALOZZI et al. "Prognostic importance of thymidylate synthase expression in early breast cancer" <i>J. Clin. Oncol.</i> (May 1997) 15(5):1923-1931	
Examiner's Signature	L. E. Crane <i>[Signature]</i>		Date Considered 09/21/2005

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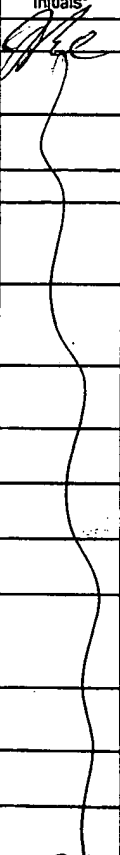

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Sheet 12 of 15

**Complete if Known**

Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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E. E. Crane

Date  
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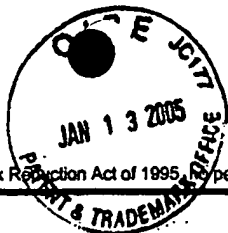
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Sheet 13 of 15

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Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --1615--
Examiner Name	Not Yet Assigned
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		Application Number	10/048,033
		Filing Date	November 28, 2002
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1623 --1615--
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<i>[Signature]</i>	192	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722	
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<i>[Signature]</i>	202	van LAAR et al. "Comparison of 5-fluoro-2'-deoxyuridine with 5-fluorouracil and their role in the treatment of colorectal cancer" <i>European J. Cancer</i> (1998) 34(3):296-306	
<i>[Signature]</i>	203	VOLM et al. "Relationship of inherent resistance to doxorubicin, proliferative activity and expression of P-glycoprotein 170, and glutathione S-transferase- $\pi$ in human lung tumors" <i>Cancer</i> (Aug. 15, 1992) 70(4):764-769	
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<i>[Signature]</i>	205	WANG et al. "Identification and characterization of Ich-3, a member of the interleukin-1 $\beta$ converting enzyme (ICE)/Ced-3 family and an upstream regulator of ICE" <i>J. Biol. Chem.</i> (Aug. 23, 1996) 271(34):20580-20587	
Examiner's Signature	L. E. Czane <i>[Signature]</i>		Date Considered 09/21/2005

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Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 -- <del>1615</del> --
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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Signature**

L. E. Crane

Date  
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**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
<i>He</i>	1	DE 32 29 169 A1	02-09-84	De Clercq et al.		
<i>He</i>	2	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	3	EP 0 311 108 A2	04-12-89	Stichting REGA VZW		
<i>He</i>	4	EP 0 316 592	05-24-89	Stichting REGA VZW		
<i>He</i>	5	GB 982 776	02-10-65	The Wellcome Foundation		
<i>He</i>	6	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
<i>He</i>	7	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
<i>He</i>	8	WO 90/03978	04-19-90	Stichting REGA VZW		
<i>He</i>	9	WO 91/17424	11-14-91	Vical, Inc.		
<i>He</i>	10	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
<i>He</i>	11	WO 93/06120	04-01-93	University of Rochester		

Examiner's  
Signature

L. E. Crane

Date  
Considered

09/21/2005

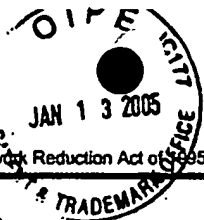
\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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\*\* Duplicate citation: see PTO-892 for citation.





Substitute for form 1449A-PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 1615 ---
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
/					

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
Me	12	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
**	13	WO 94/22483	10-13-94	Kozak, Alexander		
Me	14	WO 95/01806	01-19-95	Kondratyev, A.		
	15	WO 95/08556	03-30-95	Amersham International, Inc.		
Me	16	WO 95/12678	05-11-95	Connors, T. et al.		
**	17	WO 96/03451	02-08-96	Springer et al.		
**	18	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

Examiner's  
Signature

L. E. Crane

Date  
Considered

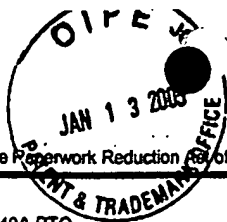
09/21/2005

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PTO/SB/08A (08-03)

Approved for use through 07/31/2008. OMB 0851-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 3 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 --4615--
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
	19	WO 96/10030	04-04-96	Isis Pharmaceuticals, Inc.		
JRC	20	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		
JRC	21	WO 96/33168	10-24-96	Kumiai Chemical Industry Co Ltd et al.		
JRC	22	WO 96/40088	12-19-96	Hostettler, Karl Y.		
	23	WO 96/40708	12-19-96	La Jolla Pharmaceuticals, Inc.		
JRC	24	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
JRC	25	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		

Examiner's  
Signature

L. E. Crane

Date  
Considered

09/21/2005

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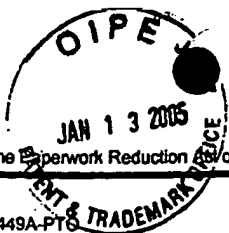
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10/048,033 - PTO-1449 #2

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 4 of 5

**Complete if Known**

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1623 ---1615---
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
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Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
**	26	WO 97/28179	08-07-97	Fick, James & Israel, Mark		
me	27	WO 97/49717	12-31-97	Balzarini et al.		
me	28	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
me	29	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
me	30	WO 99/20741	04-29-99	Geron Corporation		
me	31	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		

Examiner's  
Signature L. E. CraneDate  
Considered

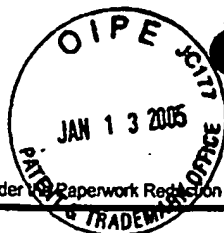
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<b>Substitute for form 1449A-PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)  Sheet 5 of 5				<b>Complete if Known</b>	
				Application Number	10/048,033
				Filing Date	November 27, 2002
				First Named Inventor	H. Michael SHEPARD
				Art Unit	1623 -- <del>1645</del> --
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	NB 2006.01

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	32	WO 99/37753	07-29-99	NewBiotics, Inc.		
	33	WO 00/18775	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	34	WO 00/33888	06-15-00	Dubois, V. et al.		
	35	WO 01/07088	02-01-01	NewBiotics, Inc.		
	36	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
	37	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

Examiner's Signature	L. E. Crane <i>[Signature]</i>	Date Considered	09/21/2005
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10/048,033 - PTO-1449 #2


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## ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18

Stylesheet Version v18.0

p.1 of 2

Title of Invention	METHODS FOR TREATING THERAPY-RESISTANT TUMORS						
<p>Application Number : 10/048033 </p> <p>Confirmation Number: 2767</p> <p>First Named Applicant: H. SHEPARD</p> <p>Attorney Docket Number: NB 2006.01</p> <p>Art Unit: <del>4645</del> / 623</p> <p>Examiner: Not Yet Assigned</p> <p>Search string: (3852266 or 4247544 or 4267171 or 4542210 or 4668777 or 4816570 or 4948882 or 4963263 or 4963533 or 4975278 or 5070082 or 5077282 or 5077283 or 5085983 or 5116822 or 5116827 or 5133866 or 5137724 or 5212161 or 5212291 or 5217869 or 5233031 or 5264618 or 5300425 or 5338659 or 5430148 or 5433955 or 5457187 or 5459127 or 5516631 or 5521161 or 5527900 or 5596018 or 5616564 or 5627165 or 5645988 or 5663321 or 5733896 or 5798340 or 5968910 or 5981507 or 6057305 or 6245750 or 6339151 or 6495553 or 20010034440 ).pn</p>							
<b>US Patent Documents</b>							
Note: Applicant is not required to submit a paper copy of cited US Patent Documents							
init	Cite.No.	Patent No.	Date	Patentee	Kind	Class	Subclass
<del>38</del>	<del>1</del>	<del>3852266</del>	<del>1974-12-03</del>	<del>Kiyonagi et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
<del>Me</del>	<del>2</del>	<del>4247544</del>	<del>1981-01-27</del>	<del>Bergstrom et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
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<del>7</del>	<del>4</del>	<del>4542210</del>	<del>1985-09-17</del>	<del>Sakata et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
<del>7</del>	<del>5</del>	<del>4668777</del>	<del>1987-05-26</del>	<del>Caruthers et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
<del>7</del>	<del>6</del>	<del>4816570</del>	<del>1989-03-28</del>	<del>Farquhar</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
<del>7</del>	<del>7</del>	<del>4948882</del>	<del>1990-08-14</del>	<del>Ruth</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
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<del>Me</del>	<del>10</del>	<del>4975278</del>	<del>1990-12-04</del>	<del>Senter et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
<del>Me</del>	<del>11</del>	<del>5070082</del>	<del>1991-12-03</del>	<del>Murdoek et al.</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
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<del>Me</del>	<del>14</del>	<del>5085983</del>	<del>1992-02-04</del>	<del>Scanlon</del>	<del>_____</del>	<del>_____</del>	<del>_____</del>
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Examiner Name L.E. CRANE				Date 09/21/2005			

\*\* Duplicate citations: see PTO-892 for citations.


10/048,033 - PTO-1449 #1

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## ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18  
Stylesheet Version v18.0

p. 2 of 2

Title of Invention		METHODS FOR TREATING THERAPY-RESISTANT TUMORS					
Application Number :		10/048033					
Confirmation Number:		2767					
First Named Applicant:		H. SHEPARD					
Attorney Docket Number:		NB 2006.01					
Art Unit:		1615 / 623					
Examiner:		Not Yet Assigned					
<del>20</del>	<del>5212291</del>	<del>1993-05-18</del>	<del>Murdock et al.</del>				
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<del>22</del>	<del>5233031</del>	<del>1993-08-03</del>	<del>Borch et al.</del>				
<del>23</del>	<del>5264618</del>	<del>1993-11-23</del>	<del>Felgner et al.</del>				
<del>24</del>	<del>5300425</del>	<del>1994-04-05</del>	<del>Kauvar</del>				
<del>25</del>	<del>5338659</del>	<del>1994-08-16</del>	<del>Kauvar et al.</del>				
<del>26</del>	<del>5430148</del>	<del>1995-07-04</del>	<del>Webber et al.</del>				
<del>27</del>	<del>5433955</del>	<del>1995-07-18</del>	<del>Bredehorst et al.</del>				
<del>28</del>	<del>5457187</del>	<del>1995-10-10</del>	<del>Gmeiner et al.</del>				
<del>29</del>	<del>5459127</del>	<del>1995-10-17</del>	<del>Felgner et al.</del>				
<del>30</del>	<del>5516631</del>	<del>1996-05-14</del>	<del>Frisch</del>				
<del>31</del>	<del>5521161</del>	<del>1996-05-28</del>	<del>Malley et al.</del>				
<del>32</del>	<del>5527900</del>	<del>1996-06-18</del>	<del>Balzarini et al.</del>				
<del>33</del>	<del>5596018</del>	<del>1997-01-21</del>	<del>Baba et al.</del>				
<del>34</del>	<del>5616564</del>	<del>1997-04-01</del>	<del>Rapaport et al.</del>				
<del>35</del>	<del>5627165</del>	<del>1997-05-06</del>	<del>Glazier</del>				
<del>36</del>	<del>5645988</del>	<del>1997-07-08</del>	<del>Vande Woude et al.</del>				
<del>37</del>	<del>5663321</del>	<del>1997-09-02</del>	<del>Gmeiner et al.</del>				
<del>38</del>	<del>5733896</del>	<del>1998-03-31</del>	<del>Holy et al.</del>				
<del>39</del>	<del>5798340</del>	<del>1998-08-25</del>	<del>Bischofberger et al.</del>				
<del>40</del>	<del>5968910</del>	<del>1999-10-19</del>	<del>Balzarini</del>				
<del>41</del>	<del>5981507</del>	<del>1999-11-09</del>	<del>Josephson et al.</del>				
<del>42</del>	<del>6057305</del>	<del>2000-05-02</del>	<del>Holy et al.</del>				
<del>43</del>	<del>6246750</del>	<del>2001-06-12</del>	<del>Shepard</del>				
<del>44</del>	<del>6339151</del>	<del>2002-02-15</del>	<del>Shepard et al.</del>				
<del>45</del>	<del>6495553</del>	<del>2002-12-17</del>	<del>Shepard</del>				

\*\* Duplicate citations: see PTO-892 for citations.

**US Published Applications**

Note: Applicant is not required to submit a paper copy of cited US Published Applications

init	Cite No.	Pub. No.	Date	Applicant	Kind	Class	Subclass
<del>58</del>	<del>1</del>	<del>20040084440</del>	<del>2001-10-25</del>	<del>Shepard et al.</del>			

**Signature**

Examiner Name	Date
L.E. CRANE	09/21/2005

\*\* Duplicate citations: see PTO-892 for citations.

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